

Date Mailed:

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Sheet 1 of 11

FORM 1449\*

## INFORMATION DISCLOSURE STATEMENT

## IN AN APPLICATION

(Use several sheets if necessary)

Docket Number:

13615.21USU1

Application Number:

09/895,871

Applicant: FANG ET AL.

Filing Date: JUNE 29, 2001

Group Art Unit: 1645.0224

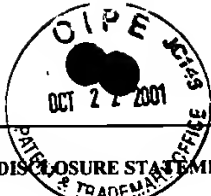
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## U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | DOCUMENT NO.    | DATE       | NAME                | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|------------------|-----------------|------------|---------------------|-------|----------|----------------------------|
| RR               | 4,224,179 (456) | 09/23/1980 | Schneider           | —     | —        |                            |
| RR               | 4,231,877 (457) | 11/04/1980 | Yamauchi et al.     | —     | —        |                            |
| RR               | 4,235,871 (447) | 11/25/1980 | Papahadjopoulos     | —     | —        |                            |
| RR               | 4,247,411 (448) | 01/27/1981 | Vanlerberghe et al. | —     | —        |                            |
| RR               | 4,394,448 (458) | 07/19/1983 | Szoka, Jr. et al.   | —     | —        |                            |
| RR               | 4,399,216 (459) | 08/16/1983 | Axel et al.         | —     | —        |                            |
| RR               | 4,522,811 (707) | 06/11/1985 | Eppstein et al.     | —     | —        |                            |
| RR               | 4,616,088 (688) | 10/07/1986 | Ryono et al.        | —     | —        |                            |
| RR               | 4,636,491 (598) | 01/13/1987 | Bock et al.         | —     | —        |                            |
| RR               | 4,665,193 (706) | 05/12/1987 | Ryono et al.        | —     | —        |                            |
| RR               | 4,668,770 (99)  | 05/26/1987 | Boger et al.        | —     | —        |                            |
| RR               | 4,673,567 (460) | 06/16/1987 | Jizomoto            | —     | —        |                            |
| RR               | 4,676,980 (461) | 06/30/1987 | Segal et al.        | —     | —        |                            |
| RR               | 4,736,866 (474) | 04/12/1988 | Leder et al.        | —     | —        |                            |
| RR               | 4,749,792 (597) | 06/07/1988 | Natarajan et al.    | —     | —        |                            |
| RR               | 4,753,788 (462) | 06/28/1988 | Gamble              | —     | —        |                            |
| RR               | 4,814,270 (463) | 03/21/1989 | Piran               | —     | —        |                            |
| RR               | 4,816,567 (464) | 03/28/1989 | Cabilly et al.      | —     | —        |                            |
| RR               | 4,870,009 (465) | 09/26/1989 | Evans et al.        | —     | —        |                            |
| RR               | 4,880,781 (13)  | 11/14/1989 | Hester, Jr. et al.  | —     | —        |                            |
| RR               | 4,897,355 (466) | 01/30/1990 | Eppstein et al.     | —     | —        |                            |
| RR               | 5,010,182 (467) | 04/23/1991 | Brake et al.        | —     | —        |                            |
| RR               | 5,142,056 (590) | 08/25/1992 | Kempe et al.        | —     | —        |                            |
| RR               | 5,145,684 (846) | 09/08/1992 | Liversidge et al.   | —     | —        |                            |
| RR               | 5,162,538 (17)  | 11/10/1992 | Voges et al.        | —     | —        |                            |
| RR               | 5,175,281 (594) | 12/29/1992 | McCall et al.       | —     | —        |                            |
| RR               | 5,250,565 (444) | 10/05/1993 | Brooks et al.       | —     | —        |                            |

## U.S. PATENT DOCUMENTS

|   |           |                 |         |
|---|-----------|-----------------|---------|
| EXAMINER  | RR Payman | DATE CONSIDERED | 6-10-03 |
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FORM 1449\*

## INFORMATION DISCLOSURE STATEMENT

## IN AN APPLICATION

(Use several sheets if necessary)

Docket Number:

13615.21USU1

Application Number:

09/895,871

Applicant: FANG ET AL.

Filing Date: JUNE 29, 2001

Group Art Unit: 1643/21

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| EXAMINER INITIAL | DOCUMENT NO.    | DATE       | NAME              | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|------------------|-----------------|------------|-------------------|-------|----------|----------------------------|
| RR               | 5,364,934 (468) | 11/15/1994 | Drayna et al.     | —     | —        |                            |
| RR               | 5,374,652 (446) | 12/20/1994 | Buzzetti et al.   | —     | —        |                            |
| RR               | 5,376,542 (469) | 12/27/1994 | Schlegal          | —     | —        |                            |
| RR               | 5,387,742 (177) | 02/07/1995 | Cordell           | —     | —        |                            |
| RR               | 5,441,870 (189) | 08/15/1995 | Seubert et al.    | —     | —        |                            |
| RR               | 5,461,067 (599) | 10/24/1995 | Norbeck et al.    | —     | —        |                            |
| RR               | 5,475,138 (556) | 12/12/1995 | Pal et al.        | —     | —        |                            |
| RR               | 5,481,011 (847) | 01/02/1996 | Chen et al.       | —     | —        |                            |
| RR               | 5,482,947 (838) | 01/09/1996 | Talley et al.     | —     | —        |                            |
| RR               | 5,502,061 (591) | 03/26/1996 | Hui et al.        | —     | —        |                            |
| RR               | 5,502,187 (595) | 03/26/1996 | Ayer et al.       | —     | —        |                            |
| RR               | 5,508,294 (837) | 04/16/1996 | Vazquez et al.    | —     | —        |                            |
| RR               | 5,510,349 (853) | 04/23/1996 | Talley et al.     | —     | —        |                            |
| RR               | 5,510,388 (703) | 04/23/1996 | Vazquez et al.    | —     | —        |                            |
| RR               | 5,516,784 (640) | 05/14/1996 | Bennett et al.    | —     | —        |                            |
| RR               | 5,521,219 (850) | 05/28/1996 | Vazquez et al.    | —     | —        |                            |
| RR               | 5,545,640 (642) | 08/13/1996 | Beaulieu et al.   | —     | —        |                            |
| RR               | 5,593,846 (201) | 01/14/1997 | Schenk et al.     | —     | —        |                            |
| RR               | 5,602,175 (542) | 02/11/1997 | Talley et al.     | —     | —        |                            |
| RR               | 5,602,169 (445) | 02/11/1997 | Hewawasam et al.  | —     | —        |                            |
| RR               | 5,604,102 (202) | 02/18/1997 | McConlogue et al. | —     | —        |                            |
| RR               | 5,610,190 (638) | 03/11/1997 | Talley et al.     | —     | —        |                            |
| RR               | 5,612,486 (185) | 03/18/1997 | McConlogue et al. | —     | —        |                            |
| RR               | 5,625,031 (470) | 04/29/1997 | Webster et al.    | —     | —        |                            |
| RR               | 5,631,405 (554) | 05/20/1997 | Pal et al.        | —     | —        |                            |
| RR               | 5,639,769 (836) | 06/17/1997 | Vazquez et al.    | —     | —        |                            |
| RR               | 5,648,511 (704) | 07/15/1997 | Ng et al.         | —     | —        |                            |
| RR               | 5,663,200 (18)  | 09/02/1997 | Bold et al.       | —     | —        |                            |
| RR               | 5,708,004 (536) | 01/13/1998 | Talley et al.     | —     | —        |                            |

EXAMINER

RR Raymond

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6-10-07

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|   |                                |                                   |
|---|--------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>13615.21USU1 | Application Number:<br>09/895,871 |
|   | Applicant: FANG ET AL.         |                                   |
|   | Filing Date: JUNE 29, 2001     | Group Art Unit: 1645/624          |

|    |                 |            |                      |   |   |  |
|----|-----------------|------------|----------------------|---|---|--|
| RR | 5,720,936 (186) | 02/24/1998 | Wadsworth et al.     | — | — |  |
| RR | 5,721,130 (184) | 02/24/1998 | Seubert et al.       | — | — |  |
| RR | 5,733,882 (29)  | 03/31/1998 | Carr et al.          | — | — |  |
| RR | 5,744,346 (182) | 04/28/1998 | Chrysler et al.      | — | — |  |
| RR | 5,753,652 (711) | 05/19/1998 | Fässler et al.       | — | — |  |
| RR | 5,760,064 (851) | 06/02/1998 | Vazquez et al.       | — | — |  |
| RR | 5,760,076 (548) | 06/02/1998 | Vazquez et al.       | — | — |  |
| RR | 5,766,846 (171) | 06/16/1998 | Schlossmacher et al. | — | — |  |
| RR | 5,807,870 (652) | 09/15/1998 | Anderson et al.      | — | — |  |
| RR | 5,807,891 (19)  | 09/15/1998 | Bold et al.          | — | — |  |
| RR | 5,811,633 (176) | 09/22/1998 | Wadsworth et al.     | — | — |  |
| RR | 5,827,891 (639) | 10/27/1998 | Dressman et al.      | — | — |  |
| RR | 5,830,897 (653) | 11/03/1998 | Vazquez et al.       | — | — |  |
| RR | 5,831,117 (547) | 11/03/1998 | Ng et al.            | — | — |  |
| RR | 5,847,169 (645) | 12/08/1998 | Nummy et al.         | — | — |  |
| RR | 5,849,911 (535) | 12/15/1998 | Fässler et al.       | — | — |  |
| RR | 5,850,003 (705) | 12/15/1998 | McLonogue et al.     | — | — |  |
| RR | 5,863,902 (428) | 01/26/1999 | Munoz et al.         | — | — |  |
| RR | 5,872,101 (429) | 02/16/1999 | Munoz et al.         | — | — |  |
| RR | 5,877,015 (710) | 03/02/1999 | Hardy et al.         | — | — |  |
| RR | 5,877,399 (178) | 03/02/1999 | Hsiao et al.         | — | — |  |
| RR | 5,912,410 (418) | 06/15/1999 | Cordell              | — | — |  |
| RR | 5,922,770 (543) | 07/13/1999 | Peschke et al.       | — | — |  |
| RR | 5,935,976 (91)  | 08/10/1999 | Bold et al.          | — | — |  |
| RR | 5,942,400 (181) | 08/24/1999 | Anderson et al.      | — | — |  |
| RR | 5,962,419 (434) | 10/05/1999 | McDonald et al.      | — | — |  |
| RR | 5,965,588 (686) | 10/12/1999 | Vazquez et al.       | — | — |  |
| RR | 6,001,813 (131) | 12/14/1999 | Gyorkos et al.       | — | — |  |
| RR | 6,013,658 (16)  | 01/11/2000 | Lau et al.           | — | — |  |
| RR | 6,022,872 (644) | 02/08/2000 | Vazquez et al.       | — | — |  |
| RR | 6,045,829 (538) | 04/04/2000 | Liversidge et al.    | — | — |  |

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| EXAMINER<br><i>RR Raymond</i>   | DATE CONSIDERED<br><i>6-10-03</i> |
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FORM 1449\*

## INFORMATION DISCLOSURE STATEMENT

IN AN APPLICATION

(Use several sheets if necessary)

Docket Number:

13615.21USU1

Application Number:

09/895,871

Applicant: FANG ET AL.

Filing Date: JUNE 29, 2001

Group Art Unit: 1628

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|    |                    |            |                 |  |  |  |
|----|--------------------|------------|-----------------|--|--|--|
| RR | 6,051,684 (427)    | 04/18/2000 | McDonald et al. |  |  |  |
| RR | 6,060,476 (637)    | 05/09/2000 | Vazquez et al.  |  |  |  |
| RR | 6,150,344 (685)    | 11/21/2000 | Carroll et al.  |  |  |  |
| RR | 6,153,652 (191)    | 11/28/2000 | Wu et al.       |  |  |  |
| RR | 6,191,166 B1 (50)  | 02/20/2001 | Audia et al.    |  |  |  |
| RR | 6,221,670 B1 (355) | 04/24/2001 | Cordell et al.  |  |  |  |

## FOREIGN PATENT DOCUMENTS

|    | DOCUMENT NO.        | DATE       | COUNTRY | CLASS | SUBCLASS | TRANSLATION |    |
|----|---------------------|------------|---------|-------|----------|-------------|----|
|    |                     |            |         |       |          | YES         | NO |
| RR | 0 036776 A2 (471)   | 09/30/1981 | Europe  |       |          |             |    |
| RR | 0 073 657 B1 (476)  | 03/09/1983 | Europe  |       |          |             |    |
| RR | 0 117 060 A2 (472)  | 08/29/1984 | Europe  |       |          |             |    |
| RR | 0 117 058 B1 (473)  | 08/29/1984 | Europe  |       |          |             |    |
| RR | 0 173 441 A1 (557)  | 05/03/1986 | Europe  |       |          |             |    |
| RR | 0 209 897 A2 (90)   | 01/28/1987 | Europe  |       |          |             |    |
| RR | 0 212 903 B1 (100)  | 03/04/1987 | Europe  |       |          |             |    |
| RR | DE 3610593 A1 (98)  | 10/01/1987 | Germany |       |          |             |    |
| RR | 0 264 106 B1 (101)  | 04/20/1988 | Europe  |       |          |             |    |
| RR | DE 3721 855 A1 (93) | 09/22/1988 | Germany |       |          |             |    |
| RR | 0 274 259 A2 (89)   | 07/13/1988 | Europe  |       |          |             |    |
| RR | 2 203 740 A (544)   | 10/25/1988 | UK      |       |          |             |    |
| RR | 2 211 504 A (475)   | 07/05/1989 | UK      |       |          |             |    |
| RR | 0 320 205 A2 (102)  | 06/14/1989 | Europe  |       |          |             |    |
| RR | 0 337 714 (8)       | 10/18/1989 | Europe  |       |          |             |    |
| RR | 0 362 179 A2 (449)  | 04/04/1990 | Europe  |       |          |             |    |
| RR | 0 372 537 A2 (96)   | 06/13/1990 | Europe  |       |          |             |    |
| RR | 0 437 729 A2 (21)   | 07/24/1991 | Europe  |       |          |             |    |
| RR | DE 40 03 575 A1     | 08/08/1991 | Germany |       |          |             |    |
| RR | 0 609 625 A1 (567)  | 08/10/1994 | Europe  |       |          |             |    |
| RR | 0 652 009 A1 (709)  | 05/10/1995 | Europe  |       |          |             |    |
| RR | 7-126286 (97)       | 05/16/1995 | Japan   |       |          |             |    |

EXAMINER

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6-10-02

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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>13615.21USUI | Application Number:<br>09/895,871    |
|   | Applicant: FANG ET AL.         |                                      |
|   | Filing Date: JUNE 29, 2001     | Group Art Unit: <del>1645</del> 1624 |

|    |                     |            |     |   |   |  |  |
|----|---------------------|------------|-----|---|---|--|--|
| RR | WO 87/02986 (551)   | 05/21/1987 | PCT | — | — |  |  |
| RR | WO 87/04349 (10)    | 07/30/1987 | PCT | — | — |  |  |
| RR | WO 87/05330 (454)   | 09/11/1987 | PCT | — | — |  |  |
| RR | WO 89/00161 (15)    | 01/12/1989 | PCT | — | — |  |  |
| RR | WO 89/01488 (12)    | 02/23/1989 | PCT | — | — |  |  |
| RR | WO 89/05859 (453)   | 06/29/1989 | PCT | — | — |  |  |
| RR | WO 90/13646 (452)   | 11/15/1990 | PCT | — | — |  |  |
| RR | WO 91/00360 (451)   | 01/10/1991 | PCT | — | — |  |  |
| RR | WO 92/00750 (537)   | 01/23/1992 | PCT | — | — |  |  |
| RR | WO 92/17490 (14)    | 10/15/1992 | PCT | — | — |  |  |
| RR | WO 92/20373 (455)   | 11/26/1992 | PCT | — | — |  |  |
| RR | WO 93/02057 (11)    | 02/04/1993 | PCT | — | — |  |  |
| RR | WO 93/08829 (450)   | 05/13/1993 | PCT | — | — |  |  |
| RR | WO 93/17003 (7)     | 09/02/1993 | PCT | — | — |  |  |
| RR | WO 94/04492 (848)   | 03/03/1994 | PCT | — | — |  |  |
| RR | WO 95/06030 (839)   | 03/02/1995 | PCT | — | — |  |  |
| RR | WO 97/30072 (22)    | 08/21/1997 | PCT | — | — |  |  |
| RR | WO 98/22597 (170)   | 05/28/1998 | PCT | — | — |  |  |
| RR | WO 98/29401 (562)   | 07/09/1998 | PCT | — | — |  |  |
| RR | WO 98/33795 (546)   | 08/06/1998 | PCT | — | — |  |  |
| RR | WO 98/50342 (550)   | 11/12/1998 | PCT | — | — |  |  |
| RR | WO 99/41266 (568)   | 08/19/1999 | PCT | — | — |  |  |
| RR | WO 99/54293 (635)   | 10/28/1999 | PCT | — | — |  |  |
| RR | WO 00/17369 (169)   | 03/30/2000 | PCT | — | — |  |  |
| RR | WO 00/47618 (364)   | 08/17/2000 | PCT | — | — |  |  |
| RR | WO 00/56335 (314)   | 09/28/2000 | PCT | — | — |  |  |
| RR | WO 00/61748 (302)   | 10/19/2000 | PCT | — | — |  |  |
| RR | WO 00/69262 (272)   | 11/23/2000 | PCT | — | — |  |  |
| RR | WO 00/77030 (256)   | 12/21/2000 | PCT | — | — |  |  |
| RR | WO 01/00663 (159)   | 01/04/2001 | PCT | — | — |  |  |
| RR | WO 01/00665 A2 (20) | 01/04/2001 | PCT | — | — |  |  |

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| EXAMINER<br><i>R. P. Rasmussen</i>  | DATE CONSIDERED<br>6-10-03 |
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|   | Applicant: FANG ET AL.         |                                      |
|   | Filing Date: JUNE 29, 2001     | Group Art Unit: <del>4645</del> 1624 |

|    |                      |            |     |   |   |  |  |
|----|----------------------|------------|-----|---|---|--|--|
| RR | WO 01/10387 A2 (443) | 02/15/2001 | PCT | — | — |  |  |
| RR | WO 01/19797 A2 (381) | 03/22/2001 | PCT | — | — |  |  |
| RR | WO 01/23533 A2 (289) | 04/05/2001 | PCT | — | — |  |  |
| RR | WO 01/29563 A1 (479) | 04/26/2001 | PCT | — | — |  |  |
| RR | WO 01/51659 A2 (790) | 07/19/2001 | PCT | — | — |  |  |
|    |                      |            |     |   |   |  |  |
|    |                      |            |     |   |   |  |  |
|    |                      |            |     |   |   |  |  |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| RR | Abbenante, et al., <i>Biochemical and Biophysical Research Communications</i> , 2000, 268, pp. 1331-35<br>Inhibitors of $\beta$ -Amyloid Formation Based on the $\beta$ -Secretase Cleavage Site [439]                            |
| RR | Alterman et al., <i>J. Med. Chem.</i> , 1998, 41, 3782-3792<br>Design and Synthesis of New Potent C <sub>2</sub> -Symmetric HIV-1 Protease Inhibitors. Use of L-Mannaric Acid as a Peptidomimetic Scaffold [868]                  |
| RR | Amblard et al., <i>J. Med. Chem.</i> , 1999, 42:20, pp. 4193-4201<br>Synthesis and Characterization of Bradykinin B <sub>2</sub> Receptor Agonists Containing Constrained Dipeptide Mimics [730]                                  |
| RR | Arrowsmith et al., <i>Tetrahedron Letters</i> , 1987, 28:45, pp. 5569-5572<br>Amino-Alcohol Dipeptide Analogues: A Simple Synthesis of a Versatile Isostere for the Development of Proteinase Inhibitors [584]                    |
| RR | Askin et al., <i>The Journal of Organic Chemistry</i> , 1992, 57:10, pp. 2771-2773<br>Highly Disastrous Alkylations of Chiral Amide Enolates: New Routes to Hydroxyethylene Dipeptide Isostere Inhibitors of HIV-1 Protease [561] |
| RR | Balicki et al., <i>Synth. Comm.</i> , 1993, 23(22), pp. 3149-3155<br>Mild and Efficient Conversion of Nitriles to Amides with Basic Urea-Hydrogen Peroxide Adduct [874]   |
| RR | Barton, <i>Protective Groups in Organic Chemistry</i> , 1976, Chpt. 2, pp. 43-93<br>Protection of N-H Bonds and NR <sub>2</sub> [718]   |
| RR | Basu et al., <i>Tetrahedron Letters</i> , 1998, 39, pp. 3005-3006<br>Efficient Transformation of Nitrile into Amide under Mild Condition [881]  |
| RR | Bennett et al., <i>Synlett</i> , 1993, 9, pp. 703-704<br>The Synthesis of Novel HIV-Protease Inhibitors via Silica Gel Assisted Addition of Amines to Epoxides [744]  |
| RR | Berge et al., <i>Journal of Pharmaceutical Sciences</i> , 1/1977, 66:1, pp. 1-19<br>Pharmaceutical Salts [735]  |
| RR | Blatt, <i>Organic Syntheses</i> , Collective Vol. 2, pp. 312-315<br>Heptaloxime [883] (no date)   |
| RR | Bodendorf et al., <i>The Journal of Biological Chemistry</i> , 2001, 276:15, pp. 12019 - 12023<br>A Splice Variant of $\beta$ -Secretase Deficient in the Amyloidogenic Processing of the Amyloid Precursor Protein [493]         |

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|---|---------------------|-----------------|---------|
| EXAMINER  | <i>R. R. Ruyner</i> | DATE CONSIDERED | 6-10-03 |
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|   | <b>Applicant:</b> FANG ET AL.         |  |
|   | <b>Filing Date:</b> JUNE 29, 2001     | <b>Group Art Unit:</b> 4645-162-1        |

|    |   |
|----|---|
| RR | Bose et al., <i>Synth. Comm.</i> , 1997, 27(18), pp. 3119 - 3123<br>A Facile Hydration of Nitriles by Dimethyldioxirane [ 876]  |
| RR | Calderwood et al., <i>Tetrahedron Letters</i> , 1997, 38:7, pp. 1241 - 1244<br>Organocerium Reactions of Benzamides and Thiobenzamides: A Direct Synthesis of Tertiary Carbinamines [741]   |
| RR | Chen et al., <i>Tetrahedron -Mannaric Acid Letters</i> , 1997, 38:18, pp. 3175 - 3178<br>A Practical Method for the Preparation of $\alpha'$ -Chloroketones of N-Carbamate Protected- $\alpha$ -Aminoacids [885]  |
| RR | Ciganek, <i>J. Org. Chem.</i> , 1992, 57:16, pp. 4521 - 4527<br>Tertiary Carbinamines by Addition of Organocerium Reagents to Nitriles and Ketimins [721]   |
| RR | Citron et al., <i>Nature</i> , 1992, 360:6405, pp. 672-674<br>Mutation of the $\beta$ -amyloid Precursor Protein in Familial Alzheimer's Disease Increases $\beta$ -Protein Production [722]  |
| RR | Cushman et al., <i>J. Med. Chem.</i> , 1997, 40:15, pp. 2323 - 2331<br>Synthesis of Analogs of 2-Methoxyestradiol with Enhanced Inhibitory Effects on Tubulin Polymerization and Cancer Cell Groth [734]  |
| RR | Deno, et al., <i>J. Am. Chem. Soc.</i> , 1970, 92:7, pp. 3700 - 3703<br>Protonated Cyclopropane Intermediates in the Reactions of Cyclopropanecarboxylic Acids [727]  |
| RR | Diedrich et al., <i>Tetrahedron Letters</i> , 1993, 34:39, pp. 6169-6172<br>Stereoselective Synthesis of A Hydroxyethylene Dipeptide Isostere [559]   |
| RR | Diercks et al., <i>J. Am. Chem. Soc.</i> , 1986, 108:11, pp. 3150-3152<br>Tris(benzocyclobutadieno)benzene, the Triangular [4]Phenylene with a Completely Bond-Fixed Cyclohexatriene Ring: Cobalt-Catalyzed Synthesis from Hexaethynylbenzene and Thermal Ring Opening to 1,2:5,6:9, 10-Tribenzo-3,4,7,8,11,12 hexadehydro[12]-annulene [728] |
| RR | Dovey et al., <i>Journal of Neurochemistry</i> , 2001, 76, pp. 173-181<br>Functional Gamma-Sec]retase Inhibitors Reduce Beta-Amyloid Peptide Levels in Brain [396]  |
| RR | Dragovich et al., <i>Journal of Medicinal Chemistry</i> , 1999, 42:7, pp. 1203-1212<br>Structure-Based Desing, Synthesis, and Biological Evaluation of Irreversible Human Rhinovirus 3C Protease Inhibitors [553]   |
| RR | Emilien, et al., <i>Neurological Review</i> , 2000, 57, pp. 454-459<br>Prospects for Pharmacological Intervention in Alzheimer Disease [723]  |
| RR | Felman et al., <i>J. Med. Chem.</i> , 1992, 35:7, pp. 1183-1190<br>Synthesis and Antiulcer Activity of Novel 5-(2-Ethenyl Substituted)-3(2H)furanones [724]   |
| RR | Games et al., <i>Letters to Nature</i> , 29/1995, 373:6514, pp. 523-527<br>Alzheimer-type Neuropathology in Transgenic Mice Overexpressing V717F $\beta$ -amyloid Precursor Protein [441]   |
| RR | Gao et al., <i>Tetrahedron Letters</i> , 1994, 50:4, pp. 979-988<br>Asymmetric Hetero Diels-Alder Reaction Catalyzed by Stable and Easily Prepared CAB Catalysts [882]  |
| RR | Getman et al., <i>J. Med. Chem.</i> , 1993, 36:2, pp. 288-291<br>Discovery of a Novel Class of Potent HIV-1 Protease Inhibitors Containing the (R)-(Hydroxyethyl)urea Isostere [732]  |
| RR | Ghosh et al., <i>J. Am. Chem. Soc.</i> , 2000, 122, pp. 3522-3523<br>Design of Potent Inhibitors for Human Brain Memapsin 2 ( $\beta$ -Secretase). [588]  |
| RR | Ghosh et al., <i>J. Med. Chem.</i> , 1993, 36, pp. 2300-2310<br>Potent HIV Protease Inhibitors: The Development of Tetrahydrofuranlylglycines as Novel P <sub>1</sub> -Ligands [869]  |

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|---|-----------------|
| EXAMINER  | DATE CONSIDERED |
| RR Payman   | 6-10-03         |
| EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant. |                 |

FORM 1449\*

## INFORMATION DISCLOSURE STATEMENT

IN AN APPLICATION

(Use several sheets if necessary)

Docket Number:

13615.21USU1

Application Number:

09/895,871

Applicant: FANG ET AL.

Filing Date: JUNE 29, 2001

Group Art Unit: 1645

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|----|--|
| RR | Gould, <i>International Journal of Pharmaceutics</i> , 1986, 33:1-3, pp. 201 - 217<br>Salt Selection for Basic Drugs [566]   |
| RR | Greene et al., <i>Protective Groups in Organic Synthesis: 2nd Ed.</i> , 1991, Chpt. 7, pp. 309-405<br>Protection for the Amino Group [747]   |
| RR | Greene, <i>Protective Groups in Organic Synthesis</i> , 1981, Chpt. 7, pp. 218-287<br>Protection for the Amino Group [719]   |
| RR | Hardy, <i>Nature Genetics</i> , 1992, 1, pp. 233-234<br>Framing $\beta$ -Amyloid [725]   |
| RR | Heck, <i>Palladium Reagents in Organic Syntheses</i> , 1985, Chpt. 8.2, pp. 342-365<br>Carbonylation of Aromatic Compounds to Acids, Acid Derivatives, Aldehydes and Ketones [870]                                     |
| RR | Henning, <i>Organic Synthesis Highlights II</i> , 1995, pp. 251 - 259<br>A. Synthetic Routes to Different Classes of Natural Products and Analogs Thereof -- Synthesis of Hydroxyethylene Isoteric Dipeptides [565]    |
| RR | Hon et al., <i>Heterocycles</i> , 1990, 31:10, pp. 1745-1750<br>The Studies of Metal Ion Catalyzed Carbon-Hydrogen Insertion of $\alpha$ -Alkoxy- $\alpha'$ -Diazoketones Derived from Mandelic and Lactic Acids [539] |
| RR | Hong et al., <i>Science</i> , 2000, 290:5489, pp. 150-153<br>Structure of the Protease Domain of Memapsin 2 ( $\beta$ -Secretase) Complexed with Inhibitor [440]   |
| RR | Hussain et al., <i>Molecular and Cellular Neuroscience</i> , 1999, 14, pp. 419-427<br>Identification of a Novel Aspartic Protease (Asp 2) as $\beta$ -Secretase [726]  |
| RR | Kabalka et al., <i>Synth. Comm.</i> , 1990, 20(10), pp. 1445-1451<br>The Transformation of Nitriles into Amides [875]  |
| RR | Kaldor et al., <i>Bioorganic and Medicinal Chemistry Letters</i> , 1995, 5:7, pp. 721-726<br>Isophthalic Acid Derivatives: Amino Acid Surrogates for the Inhibition of HIV-1 Protease [587]                            |
| RR | Kang et al., <i>Nature</i> , 1987, 325:6106, pp. 733-736<br>The Precursor of Alzheimer's Disease Amyloid A4 Protein Resembles a Cell-Surface Receptor [505]  |
| RR | Kitaguchi et al., <i>Nature</i> , 2/11/1988, 331:6156, pp. 530-532<br>Novel Precursor of Alzheimer's Disease Amyloid Protein Shows Protease Inhibitory Activity [736]  |
| RR | Klumpp et al., <i>J. Am. Chem. Soc.</i> , 1979, 101:23<br>Lithiation of Cyclopropylcarbinols [871]   |
| RR | Lakouraj et al., <i>Indian Journal of Chemistry</i> , 1999, 38B, pp. 974-975<br>Selective Conversion of Nitriles to Amides by Amberlyst A-26 Supported Hydroperoxide [879]   |
| RR | Larock, <i>Comprehensive Organic Transformations</i> , 1986, Chpt 4, pp. 972-985<br>Carboxylic Acids to Amides [555]   |
| RR | Li et al., <i>Nature</i> , 2000, 405, pp. 689-694<br>Photoactivated V-secretase Inhibitors Directed to the Active Site Covalently Label Presenilin 1 [24]  |
| RR | Li et al., <i>Nature</i> , 2000, 405:6787, pp. 689-694<br>Photoactivated Gamma-Secretase Inhibitors Directed to the Active Site Covalently Label Presenilin 1. [585]   |

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RR [Signature]

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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>13615.21USU1 | Application Number:<br>09/895,871    |
|   | Applicant: FANG ET AL.         |                                      |
|   | Filing Date: JUNE 29, 2001     | Group Art Unit: <del>1645</del> 1624 |

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| RR | Lin et al., <i>PNAS</i> , 2000, 97:4, pp. 1456-1460<br>Human Aspartic Protease Memapsin 2 Cleaves the $\beta$ -Amyloid Precursor Protein [687]  |
| RR | Luly et al., <i>Journal of Organic Chemistry</i> , 1987, 52:8, pp. 1487-1492<br>A Synthesis of Protected Aminoalkyl Epoxides from Alpha Amino Acids [558]   |
| RR | Luo et al., <i>Nature Neuroscience</i> , 3/2001, 4:3, pp. 231-232<br>Mice Deficient in BACE1, the Alzheimer's $\beta$ -secretase, have Normal Phenotype and Abolished $\beta$ -amyloid Generation [210]   |
| RR | March, <i>Advanced Organic Chemistry: Reactions, Mechanisms, and Structure</i> , 3d Ed., pp. 380-381<br>Aliphatic Nucleophilic Substitution [729] 1985  |
| RR | Martin et al., <i>Tetrahedron Letters</i> , 1998, 39, pp. 1517-1520<br>Application of Almez-Mediated Amidation Reactions to Solution Phase Peptide Synthesis [540]  |
| RR | Mashraqui et al., <i>J. Am. Chem. Soc.</i> , 1982, 104, pp. 4461-4465<br>Cyclophanes. 14. Synthesis, Structure Assignment, and Conformational Properties of [2.2](2,5)Oxazolo- and Thiazolophanes [872]   |
| RR | McLendon et al., <i>The FASEB Journal</i> , 2000, 14:15, pp. 2383-2386<br>Cell-Free Assays for Gamma-Secretase Activity [359]   |
| RR | Miyaura et al., <i>Chem. Rev.</i> , 1995, 95, pp. 2457-2483<br>Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds [720]  |
| RR | Moersch et al., <i>Synthesis</i> , 1971, 12, pp. 647-649<br>The Synthesis of Alpha-Hydroxycarboxylic Acids by Acration of Lithiated Carboxylic Acids in Tetrahydrofuran Solution [564]  |
| RR | Murahashi et al., <i>J. Org. Chem.</i> , 1992, 57:9, pp. 2521-2523<br>Ruthenium-Catalyzed Hydration of Nitriles and Transformation of $\delta$ -Keto Nitriles to Ene-Lactams [877]  |
| RR | Norman et al., <i>J. Med. Chem.</i> , 2000, 43, pp. 4288-4312<br>Structure-Activity Relationships of a Series of Pyrrolo[3,2-d]pyrimidine Derivatives and Related Compounds as Neuropeptide Y5 Receptor Antagonists [867]                                   |
| RR | Owa et al., <i>J. Med. Chem.</i> , 1999, 42, pp. 3789-3799<br>Discovery of Novel Antitumor Sulfonamides Targeting G1 Phase of the Cell Cycle [866]  |
| RR | Pirttila et al., <i>Neuroscience Letter</i> , 1998, 249, pp. 21-24<br>Longitudinal Study of Cerebrospinal Fluid Amyloid Proteins and Apolipoprotein E in Patients with Probable Alzheimer's Disease [738]   |
| RR | Reetz et al., <i>Tetrahedron Letters</i> , 30:40, pp. 5425-5428<br>Protective Group Tuning in the Stereoselective Conversion of $\alpha$ -Amino Aldehydes into Aminoalkyl Epoxides [884] 1989   |
| RR | Sabbagh et al., <i>Alzheimer's Disease Review</i> , 1997, 3, 1-19<br>$\beta$ -Amyloid and Treatment Opportunities for Alzheimer's Disease [589]   |
| RR | Sakurai et al., <i>Chemical &amp; Pharmaceutical Bulletin</i> , 1993, 41:8, pp. 1378-1386<br>Studies of HIV-1 Protease Inhibitors. II, Incorporation of Four Types of Hydroxyethylene Dipeptide Isosteres at the Scissile Site of Substrate Sequences [549] |
| RR | Sakurai et al., <i>Tetrahedron Letters</i> , 1993, 34:10, pp. 5939-5942<br>A New Synthetic Route for the Gamma-Lactone Precursors of Hydroxyethylene Dipeptide Isosteres [563]  |

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| EXAMINER  | RR [Signature] | DATE CONSIDERED | 8/2/01 [Signature] |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>13615.21USU1 | Application Number:<br>09/895,871 |
|   | Applicant: FANG ET AL.         |                                   |
|   | Filing Date: JUNE 29, 2001     | Group Art Unit: 1600/2900         |

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| RR | Sebti et al., <i>Tetrahedron Letters</i> , 1996, 37:36, pp. 6555-6556<br>Catalyse Heterogene de L'Hydratation des Nitriles en Amides par le Phosphate Naturel Dope par KF et le Phosphate Trisodique [878]                                       |
| RR | Selkoe, <i>Nature</i> , 1999, 399:6738, pp. A23-A31<br>Translating Cell Biology into Therapeutic Advances in Alzheimer's Disease [541]   |
| RR | Selkoe, <i>Neuron</i> , 1991, 6:4, pp. 487-498<br>The Molecular Pathology of Alzheimer's Disease [742]   |
| RR | Seubert, et al., <i>Nature</i> , 9/1992, 359:6393, pp. 325327<br>Isolation and Quantification of Soluble Alzheimer's $\beta$ -peptide from Biological Fluids [503]   |
| RR | Shearman et al., <i>Biochemistry</i> , 2000, 39, pp. 86989704<br>L-685, 458, an Aspartyl Protease Transition State Mimic, is a Potent Inhibitor of Amyloid $\beta$ -Protein Precursor $\gamma$ -Secretase Activity [394]                         |
| RR | Shibata et al., <i>Tetrahedron Letters</i> , 1997, 38:4, pp. 619-620<br>An Expedient Synthesis of (2R,3S)-3-tertButoxycarbonylamino-1-isobutylamino-4-phenyl-2-butanol, a Key Building Block of HIV Protease Inhibitors [583]                    |
| RR | Sinha, et al., <i>Nature</i> , 12/2/1999, 402:6761, pp. 537540<br>Purification and Cloning of Amyloid Precursor Protein $\beta$ -secretase from Human Brain [743]  |
| RR | Smith et al., <i>Advanced Organic Chemistry - Reactions, Mechanisms and Structure</i> , 2001, 5ed., Chpt. 19, pp. 1552-1554<br>Reduction of Carboxylic Acids and Esters to Alkanes [919]   |
| RR | Snyder et al., <i>J. Am. Chem. Soc.</i> , Jan - Jun 1938, pp. 105-111<br>Organoboron Compounds, and the Study of Reaction Mechanisms. Primary Aliphatic Boronic Acids [873]  |
| RR | Thurkauf et al., <i>J. Med. Chem.</i> , 1990, 33, 1452-1458<br>Synthesis and Anticonvulsant Activity of 1-Phenylcyclohexylamine Analogues [749]  |
| RR | Tucker et al., <i>J. Med. Chem.</i> , 1992, 35:14, pp. 2525-2533<br>A Series of Potent HIV-1 Protease Inhibitors Containing a Hydroxyethyl Secondary Amine Transition State Isostere: Synthesis, Enzyme Inhibition, and Antiviral Activity [731] |
| RR | Vassar et al., <i>Science</i> , 10/22/1999, 286:5440, pp. 735-741<br>$\beta$ -Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE [750]  |
| RR | Vazquez et al., <i>J. of Med. Chem.</i> , 1995, 38:4, pp. 581-584<br>Inhibitors of HIV-1 Protease Containing the Novel and Potent $\Phi$ -Hydroxyethyl)sulfonamide Isostere [582]  |
| RR | Wang et al., <i>Synlett</i> , 6/2000, 6, pp. 902-904<br>Preparation of $\alpha$ -Chloroketones by the Chloroacetate Claisen Reaction [886]   |
| RR | Werner et al., <i>Organic Syntheses</i> , 1973, Collective Vol. 5, pp. 273-276<br>Cyclobutylamine* [752]   |
| RR | Wilgus, et al., <i>Tetrahedron Letters</i> , 1995, 36:20, pp. 3469-3472<br>The Acid-Catalyzed and Uncatalyzed Hydrolysis of Nitriles on Unactivated Alumina [880]  |
| RR | Yan et al., <i>Nature</i> , 12/1999, 402:6761, pp. 533-537<br>Membrane-anchored Aspartyl Protease with Alzheimer's Disease $\beta$ -secretase Activity [753]   |

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| EXAMINER  | DATE CONSIDERED |
| RR  | 6-10-03         |
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FORM 1449\*

## INFORMATION DISCLOSURE STATEMENT

IN AN APPLICATION

(Use several sheets if necessary)

Docket Number:

13615.21USU1

Application Number:

09/895,871

Applicant: FANG ET AL.

Filing Date: JUNE 29, 2001

Group Art Unit: ~~1645~~ 1624

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Atty. Docket No.

Serial No.

01-1693-F

09/895,871

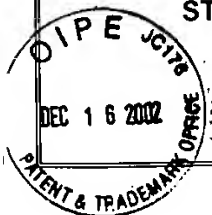
INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

Applicant: Fang, et al.

Filing Date:

June 29, 2001

Group: 1645

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## FOREIGN PATENT DOCUMENTS

| Examiner Initial | No. | Document Number | Date     | Country | Class | Subclass | Translation |    |
|------------------|-----|-----------------|----------|---------|-------|----------|-------------|----|
|                  |     |                 |          |         |       |          | Yes         | No |
| RR ✓             | 1.  | WO 99/65870     | 12/23/99 | PCT     | —     | —        |             |    |
| RR ✓             | 2.  | WO 96/22287     | 7/25/96  | PCT     | —     | —        |             |    |
| RR ✓             | 3.  | EP 0, 432, 694  | 6/19/91  | Europe  | —     | —        |             |    |

## OTHER DOCUMENTS - Including Author, Title, Date, Pertinent Pages, Etc.

| Examiner Initial | No. |   |
|------------------|-----|---|
| RR ✓             | 4.  | Chevallier N. et al., Cathepsin D displays in vitro $\beta$ -secretase-like specificity, Brain Research 750 (1997), pages 11-19   |
| RR ✓             | 5.  | Kick E.K. et al., Structure-based design and combinatorial chemistry yield low nanomolar inhibitors of cathepsin D, Chemistry and Biology, April 1997, 4:297-307  |
| RR ✓             | 6.  | Ng J.S. et al., A practical synthesis of an HIV protease inhibitor intermediate - Diastereoselective epoxide formation from chiral $\alpha$ -aminoaldehydes, Tetrahedron Vol 51, No 23, pages 6397-6410, 1995 |

Examiner

RR [Signature]

Date Considered

6-10-03

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Atty. Docket No.

01-1693-F

Serial No.

09/895,871



INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Applicant:

Fang et al.

Filing Date:

June 29, 2001

Group:

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FOREIGN PATENT DOCUMENTS

|           |   | Document Number | Date        | Country | Class | Subclass | Translation |    |
|-----------|---|-----------------|-------------|---------|-------|----------|-------------|----|
|           |   |                 |             |         |       |          | Yes         | No |
| of record | ✓ | WO 99/65870     | 23 Dec 1999 | PCT     |       |          |             |    |
|           | ✓ | WO 96/22287     | 26 Jul 1996 | PCT     |       |          |             |    |
|           | ✓ | EP 0,432,694    | 19 Jun 1991 | Europe  |       |          |             | X  |

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

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| of record | ✓ | Chevallier N. et al., Cathepsin D displays in vitro $\beta$ -secretase-like specificity, Brain Research 750 (1997), pages 11-19  |
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|           | ✓ | Ng J.S. et al., A practical synthesis of an HIV-protease inhibitor intermediate—Diastereoselective epoxide formation from chiral $\alpha$ -aminoaldehyde, Tetrahedron Vol 51, No 23, pages 6397-6410, 1995 |

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